

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
15 January 2004 (15.01.2004)

PCT

(10) International Publication Number
WO 2004/005286 A3

(51) International Patent Classification⁷: **C07D 471/04**,
A61K 31/437, A61P 31/12 // (C07D 471/04, 235:00,
221:00)

(21) International Application Number:
PCT/BE2003/000117

(22) International Filing Date: 3 July 2003 (03.07.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0215293.2 3 July 2002 (03.07.2002) GB
0313251.1 10 June 2003 (10.06.2003) GB

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicants (*for all designated States except US*): **K.U.LEUVEN RESEARCH & DEVELOPMENT** [BE/BE]; Groot Begijnhof, Benedenstraat 59, B-3000 Leuven (BE). **GILEAD SCIENCES, INC.** [US/US]; 333 Lakeside Drive, Foster City, CA 94404 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **NEYTS, Johan** [BE/BE]; Heidebergstraat 278, B-3010 Kessel-Lo (BE). **PÜRSTINGER, Gerhard** [AT/AT]; Roseggerstrasse 12, A-6020 Innsbruck (AT). **DE CLERCQ, Erik** [BE/BE]; Parklaan 9, B-3360 Lovenjoel (BE).

(74) Agents: **BIRD, William, E.** et al.; Bird Goën & Co, Klein Dalenstraat 42A, B-3020 Winksele (BE).

Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

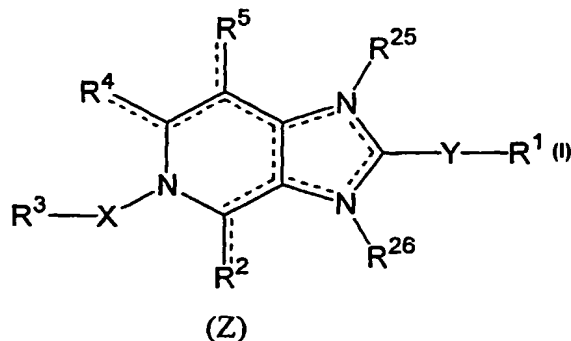
Published:

— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
18 March 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: VIRAL INHIBITORS



(57) Abstract: The present invention relates to a pharmaceutical composition for the treatment or prevention of viral infections comprising as an active principle at least one imidazo[4,5-c]pyridine derivative having the general formula (Z): (formula). The invention also relates to processes for the preparation of compounds according to the invention having above mentioned general formula and their use as a medicine or to treat or prevent viral infections.

WO 2004/005286 A3

From the INTERNATIONAL SEARCHING AUTHORITY

PCTNOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

To:

BIRD GOËN & CO
Attn. Bird, William E.
Klein Dalenstraat 42A
B-3020 Winksele
BELGIUM

RECEIVED

05 JAN. 2004

Date of mailing
(day/month/year)

05/01/2004

Applicant's or agent's file reference

K2500-PCT

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/BE 03/00117

International filing date
(day/month/year)

03/07/2003

Applicant

K.U. LEUVEN RESEARCH & DEVELOPMENT

- 1.
- ☒
- The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.**Where?** Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

- 2.
- ☐
- The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

- 3.
- ☐
- With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

- 4.
- Further action(s):**
- The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority

European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

John De Bruijn

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference K2500-PCT	FOR FURTHER ACTION <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. PCT/ BE 03/ 00117	International filing date (day/month/year) 03/07/2003	(Earliest) Priority Date (day/month/year) 03/07/2002
Applicant K.U. LEUVEN RESEACH & DEVELOPMENT		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE 03/00117

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D471/04 A61K31/437 A61P31/12 //(C07D471/04,235:00,
221:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB 2 158 440 A (ERBA FARMITALIA) 13 November 1985 (1985-11-13) page 4, line 3 -page 7; claims 1,9 ---	1
A	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; YUTILOV, YU. M. ET AL: "Synthesis and antiviral activity of spinaceamine" retrieved from STN Database accession no. 110:165603 XP002265211 abstract & KHI MIKO-FARMATSEVTICHESKII ZHURNAL, vol. 23, no. 1, 1989, pages 56-9. --- -/--	1

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

16 December 2003

Date of mailing of the international search report

05/01/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Alfaro Faus, I

INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE 03/00117

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; HORVATH, A. ET AL.: "Preparation of sunstituted nitrogen-containing heterocyclic compounds" retrieved from STN Database accession no. 132:222537 XP002265212 RN=261379-92-4 & HU 78 019 A (HORVATH) 28 May 1999 (1999-05-28) ---	7
X	WO 99 27929 A (MERCK) 10 June 1999 (1999-06-10) example 4 (6) ---	7
X	WO 96 11192 A (SEARLE) 18 April 1996 (1996-04-18) page 207, example 358c ---	7
X	WO 96 12703 A (SEARLE) 2 May 1996 (1996-05-02) examples 11,18 ---	7
X	US 5 302 601 A (KHANNAL ISH K ET AL) 12 April 1994 (1994-04-12) examples ---	7
X	EP 0 344 414 A (SEARLE & CO) 6 December 1989 (1989-12-06) examples ---	7
X	WO 95 16687 A (ABBOTT LAB) 22 June 1995 (1995-06-22) examples ---	7
P, X	HISASHI AKAMATSU ET AL.: "New efficient route for solid-phase synthesis of benzimidazole derivatives" JOURNAL OF COMBINATORIAL CHEMISTRY., vol. 4, no. 5, 2002, pages 475-483, XP002265210 AMERICAN CHEMICAL SOCIETY, WASHINGTON., US ISSN: 1520-4766 pages 479, 480, compounds 15,16(21), 16(22) -----	7

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 7-14 (in part)

Present claims 7-14 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds of formula I described in page 19, line 15 - page 22, line 9.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/BE 03/00117

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 7-14 (in part)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/BE 03/00117

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
GB 2158440	A	13-11-1985	BE 902611 A1 DE 3521303 A1 JP 61167687 A	30-09-1985 31-10-1985 29-07-1986
HU 78019	A	28-05-1999	HU 78019 A2	28-05-1999
WO 9927929	A	10-06-1999	US 6015817 A AU 1611099 A CA 2311923 A1 EP 1035850 A1 WO 9927929 A1	18-01-2000 16-06-1999 10-06-1999 20-09-2000 10-06-1999
WO 9611192	A	18-04-1996	US 5585492 A AT 224381 T AU 3686595 A CA 2202371 A1 DE 69528287 D1 DE 69528287 T2 DK 804427 T3 EP 1221441 A2 EP 0804427 A1 ES 2183886 T3 JP 10512848 T PT 804427 T WO 9611192 A1 US 5719306 A	17-12-1996 15-10-2002 02-05-1996 18-04-1996 24-10-2002 31-07-2003 27-01-2003 10-07-2002 05-11-1997 01-04-2003 08-12-1998 31-01-2003 18-04-1996 17-02-1998
WO 9612703	A	02-05-1996	US 5635514 A AU 3684795 A WO 9612703 A1 US 5688822 A	03-06-1997 15-05-1996 02-05-1996 18-11-1997
US 5302601	A	12-04-1994	US 4914108 A US 5019581 A US 5227384 A AT 112774 T AU 3127089 A CA 1337072 C DE 68918755 D1 DE 68918755 T2 DK 121189 A EP 0344414 A1 ES 2061753 T3 FI 891200 A , B, JP 1316378 A JP 2714426 B2 NO 891058 A , B, NZ 228336 A PH 26967 A ZA 8901926 A PT 90208 A	03-04-1990 28-05-1991 13-07-1993 15-10-1994 14-09-1989 19-09-1995 17-11-1994 09-03-1995 15-09-1989 06-12-1989 16-12-1994 15-09-1989 21-12-1989 16-02-1998 15-09-1989 29-01-1992 28-12-1992 30-05-1990 10-11-1989
EP 0344414	A	06-12-1989	US 4914108 A US 5019581 A AT 112774 T AU 3127089 A CA 1337072 C DE 68918755 D1	03-04-1990 28-05-1991 15-10-1994 14-09-1989 19-09-1995 17-11-1994

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/BE 03/00117

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0344414	A	DE 68918755 T2	09-03-1995
		DK 121189 A	15-09-1989
		EP 0344414 A1	06-12-1989
		ES 2061753 T3	16-12-1994
		FI 891200 A ,B,	15-09-1989
		JP 1316378 A	21-12-1989
		JP 2714426 B2	16-02-1998
		NO 891058 A ,B,	15-09-1989
		NZ 228336 A	29-01-1992
		PH 26967 A	28-12-1992
		US 5227384 A	13-07-1993
		US 5302601 A	12-04-1994
		ZA 8901926 A	30-05-1990
		PT 90208 A	10-11-1989
WO 9516687	A	22-06-1995	
		US 5486525 A	23-01-1996
		AT 212992 T	15-02-2002
		AU 690620 B2	30-04-1998
		AU 1303695 A	03-07-1995
		BR 1100809 A3	23-11-1999
		CA 2176247 A1	22-06-1995
		DE 69429827 D1	21-03-2002
		DE 69429827 T2	21-11-2002
		DK 734386 T3	27-05-2002
		EP 0734386 A1	02-10-1996
		ES 2173171 T3	16-10-2002
		JP 9507474 T	29-07-1997
		PT 734386 T	31-07-2002
		WO 9516687 A1	22-06-1995

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

☐ BLACK BORDERS

☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES

☒ FADED TEXT OR DRAWING

☒ BLURRED OR ILLEGIBLE TEXT OR DRAWING

☐ SKEWED/SLANTED IMAGES

☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS

☐ GRAY SCALE DOCUMENTS

☒ LINES OR MARKS ON ORIGINAL DOCUMENT

☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.